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|------------------------|---------------------|--|--|--|
| Application Number     | 10/000,113          |  |  |  |
| Filing Date            | October 30, 2001    |  |  |  |
| First Named Inventor   | Grant L. Schoenhard |  |  |  |
| Group Art Unit         | 1618                |  |  |  |
| Examiner Name          | Vickie Y. Kim       |  |  |  |
| Attorney Docket Number | 12971US04           |  |  |  |

|          | U.S. PATENT DOCUMENTS |   |                  |                             |   |  |  |  |
|----------|-----------------------|---|------------------|-----------------------------|---|--|--|--|
| Examiner | Cite                  | Document Number                             | Publication Date | Name of Patentee or         | Pages, Columns, Lines, Where                    |  |  |  |
| Initial* | No. <sup>1</sup>      | Number-Kind Code <sup>2</sup><br>(if known) | MM-DD-YYYY       | Applicant of Cited Document | Relevant Passages or Relevant<br>Figures Appear |  |  |  |
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|           | A11                      |   |                  |                             |   |           |  |  |  |
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|                    |              | OTHER ART NON PATENT LITERATURE DOCUMENTS  |
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| Examiner Initials* | Cite<br>No.1 | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published |
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE Under the Paperwork Reduction act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number. Complete if Known for form 1449A/PTO **Application Number** 10/000,113 Filing Date October 30, 2001 INFORMATION DISCLOSURE Grant L. Schoenhard **First Named Inventor** STATEMENT BY APPLICANT **Group Art Unit** 1618 **Examiner Name** Vickie Y. Kim (use as many sheets as necessary) 12971US04 Attorney Docket Number Sheet 2 of **U.S. PATENT DOCUMENTS** Pages, Columns, Lines, Where **Document Number** Examiner Cite **Publication Date** Name of Patentee or Relevant Passages or Relevant Number-Kind Code MM-DD-YYYY **Applicant of Cited Document** No.1 Initial\* Figures Appear (if known) Α **FOREIGN PATENT DOCUMENTS** Pages, Columns, Lines, Foreign Patent Document **Publication Date** Examiner Cite Name of Patentee or Where Relevant Passages MM-DD-YYYY Applicant of Cited Document Initials' No. Country Code<sup>3</sup>-Number <sup>4</sup>-Kind Code <sup>6</sup> (if known) or Relevant Figures Appear В OTHER ART -- NON PATENT LITERATURE DOCUMENTS Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the Examiner Cite item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue Initials\* No. number(s), publisher, city and/or country where published C<sub>1</sub> Zhen-Li Liu, et al., "Persistent reversal of P-glycoprotein-mediated daunorubicin resistance by tetrandrine in multidrug-resistant human T lymphoblastoid leukemia MOLT-4 cells," Journal of Pharmacy and Pharmacology, 55:1531-1537 (2003). C2 Hiroyuki Kusuhara, et al., "Role of transporters in the tissue-selective distribution and elimination of drugs:transporters in the liver, small intestine, brain and kidney," Journal of Controlled Release, 78:43-54 (2002). Editorial, "Membrane Transporters," European Journal of Pharmaceutical Sciences, 21:1 (2004). **C3** Haiying Sun, et al. "Drug efflux transporters in the CNS," Advanced Drug Delivery Reviews, 55:83-105 C5 Richard B. Kim, "Pharmacogenetics of CYP enzymes and drug transporters:remarkable recent advances," Advanced Drug Delivery Reviews, 54:1241-1242 (2002). C6 Tetsuya Terasaki, et al., "The blood-brain barrier efflux transporters as a detoxifying system for the brain," Advanced Drug Delivery Reviews, 36:195-209 (1999). **C7** Akira Tsuji, et al., "Carrier-mediated or specialized transport of drugs across the blood-brain barrier," Advanced Drug Delivery Reviews, 36:277-290 (1999). Massimo Rizzi, et al., "Limbic Seizures Induce P-Glycoprotein in Rodent Brain: Functional Implications **C8** for Pharmacoresistance," The Journal of Neuroscience, 22(14):5833-5839 (July 15, 2002). Astrid A. Ruefli, et al., "HMB A induces activation of a caspase-independent cell death pathway to C9 overcome P-glycoprotein-mediated multidrug resistance," Blood, Vol. 95, No. 7, 2378-2385 (April 1, 2000). C10 'Mark J. Smyth, et al., "The drug efflux protein, P-glycoprotein, additionally protects drug-resistant tumor cells from multiple forms of caspase-dependent apoptosis," Proc. Natl. Acad. Sci. USA, Vol. 95:7024-7029 (June 1998)) Miki Susanto, et al. "Cap the Enhanced Renal Clearance of Antibodies in Cystic Fibrosis Patients be C11 Explained by P-Glycoprotein Transport?," Pharmaceutical Research, Vol. 19, No. 4, 457-462 (April, 2002).

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|                      |   |  | U.S. PATENT DO                 | CUMENTS   |   |  |  |
|----------------------|---|--|--------------------------------|---|---|--|--|
| Examiner<br>Initial* | Cite<br>No. <sup>1</sup>  | Document Number  Number-Kind Code 2  (if known)  | Publication Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document                    | Pages, Columns, Lines, Where<br>Relevant Passages or Relevant<br>Figures Appear |  |  |
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